Creutzfeldt-Jakob Disease: Correlation of Focal Electroencephalographic Abnormalities and Clinical Signs

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ABSTRACT: Three patients are described with pathologically verified Creutzfeldt-Jakob disease (CJD) who presented with localizing clinical signs accompanied by focal electroencephalographic abnormalities including periodic lateralized epileptiform discharges (PLEDS). With further progression of the disease, diffuse background slowing and continuous bisynchronous periodic discharges appeared in all three cases. There was good correlation between the initial focal clinical manifestations and the EEG findings.

RÉSUMÉ: Maladie du Creutzfeldt et Jakob: corrélation entre des anomalies focales de l'électroencéphalogramme et des données cliniques. Description de 3 cas de maladie de Creutzfeldt-Jakob verifiés à la pathologie et qui se sont présentés initialement avec des signes cliniques de localisation accompagnés d'anomalies électroencéphalographiques incluant des décharges périodiques latéralisées de type épileptique. Avec la progression de la maladie, un ralentissement diffus du rythme de fond et des décharges périodiques bisynchrones continuelles sont apparues chez les trois patients. Il existait une bonne corrélation entre les manifestations cliniques focales initiales et les constatations électroencéphalographiques.

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The typical electroencephalographic abnormalities in CJD were first described by Jones and Nevin,[1] and have since been well summarized by others.[2-4] The initial abnormality is diffuse or lateralized slowing of background. Eventually bilateral diffuse high voltage periodic sharp waves, triphasic waves, or spike and wave complexes appear. Initially, the periodic complexes may be intermittent but later become continuous with a periodicity of around one per second. As the disease reaches its terminal stages, the periodic complexes may become less frequent and of lower amplitude superimposed on a slower and lower voltage background.

Focal EEG abnormalities including slowing and periodic lateralized epileptiform discharges (PLEDS) may occur in the early course of the disease, but this is not widely recognized.[2,5-7] However, if they do occur in association with focal clinical symptoms and signs, the diagnosis of CJD may not be considered, especially if dementia is absent or is not a prominent symptom. Recently, we have encountered three patients who presented with focal clinical signs and corresponding EEG abnormalities.

Case Reports

Case 1 A 67 year old woman with a past history of hypertension presented with a three-day history of difficulty with speech and a coarse tremor of her right arm. The family revealed that she had been unwell in a non-specific manner for several months.

On examination, the patient was alert and manifested a mild aphasia with poor repetition. Cranial nerve function was normal. Examination of the extremities revealed a coarse high amplitude pseudoathetotic tremor of the right arm associated with impaired joint position sense and stereognosis. There was sensory inattention involving the right arm and leg, and the right plantar response was extensor. A computerized tomogram (CT) of the brain revealed mild diffuse cerebral atrophy.

The first EEG on the day of admission showed low- to medium-voltage regular 9 - 10 Hz activity better formed on the right with lower amplitude beta on the left. Polymorphic arrythmic delta activity was lateralized to the left hemisphere. Focal intermittent irregularly recurring 0.8 - 1 Hz sharp wave complexes arose from the left parietal-posterior temporal location (Figure 1A).

The patient's neurologic status remained stable for several weeks after which she showed a progressive deterioration with a decreasing level of consciousness and bilateral myoclonic movements. Muscle tone and reflexes became increased bilaterally with bilateral extensor

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plantar responses. An EEG done 23 days after the initial record revealed periodic 0.5 - 1.5 Hz bisynchronous sharp and triphasic waves. No electrographic change was seen in association with spontaneous right arm or leg myoclonic jerking. The myoclonus was not stimulus sensitive. There was 5 - 7 Hz background activity intermixed with 2.5 Hz diffuse polymorphic delta rhythm.

The final recording on the 27th hospital day, when the patient was stuporous with constant myoclonic jerking, showed a temporal relationship between the movements and the periodic complexes, the latter preceding or more frequently coinciding with the myoclonus (Figure 1B). The voltage of the background rhythm was further reduced.

The patient died 2 ½ months after the onset of the illness. Autopsy revealed spongiform degeneration and neuronal loss consistent with CJD.

Case 2 A 73 year old man was well until three months prior to admission when he began to experience intermittent confusion, clumsiness of his left hand and an unsteady gait with a tendency to bump into objects on his left side. On examination one month later, the patient was inattentive, disoriented, and demonstrated a mild deficit in recent memory and calculation. Cranial nerve function was normal apart from a left visual field neglect. He had pseudoathetotic posturing of the left arm associated with mild weakness and increased reflexes. With testing of the left hand, there were mirror movements on the right. The sensory exam was normal. The gait was wide-based with a tendency to fall to the left. Skull radiograms and a CT scan of the brain were normal. An EEG showed a 10 Hz left occipital background rhythm and a 1.5 Hz polymorphic right occipital dominant delta. On a single occasion, left hand jerking was associated with rhythmic 3 Hz activity in the right temporal region.

There was progressive deterioration with increasing confusion and one week prior to admission, the patient experienced episodic involuntary deviation of his head and eyes to the left. On admission the patient was drowsy and oriented only to place. Speech was normal. There were frequent brief adversive seizures characterized by deviation of his head and eyes to the left with some spread of the clonic activity to the

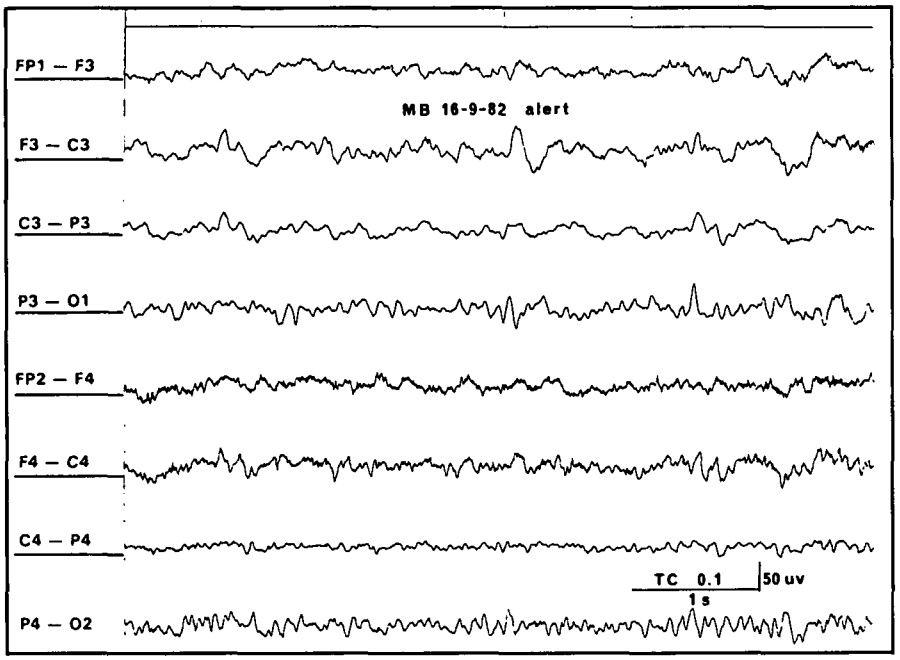

Figure 1 — Case 1
(A) Initial EEG showing polymorphic delta activity lateralized to the left hemishere and occasional low amplitude irregular, 0.8 - 1 Hz, recurrent sharp waves.

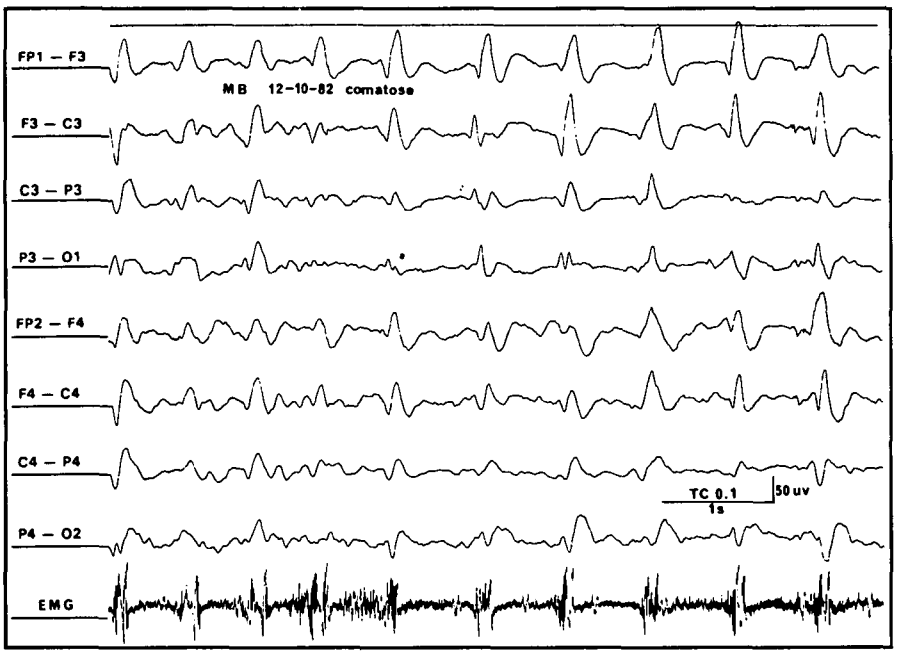

Figure 1 — Case 1
(B) Repeat recording on the 27th hospital day showing bilateral periodic complexes preceding or coinciding with the myoclonic movements seen in the EMG recording.

left arm and leg. There were also occasional bilateral multifocal myoclonic movements. The cranial nerve examination was normal apart from a left homonymous hemianopsia. There was a mild left hemiparesis with increased reflexes on the right, a marked intention tremor of the left arm and bilateral extensor plantar responses. The gait was ataxic with a tendency to fall to the left. Cerebrospinal fluid was normal. An EEG on the day of admission revealed 10 Hz, low voltage background rhythm, represented more clearly in the left hemisphere, and a dominant 5 Hz rhythm on the right. Occasional periodic sharp waves were localized in the right occipital region (Figure 2A). There was no electrographic correlate to the generalized myoclonus.

He deteriorated rapidly and within one week, he was mute and experiencing frequent bilateral adversive seizures and stimulus sensitive multifocal myoclonic movements. An EEG one month after admission showed continuous bilateral periodic 0.8 - 1 Hz synchronous epileptiform complexes (Figure 2B) attenuated only by eye opening. Brief 10 - 11 Hz low voltage activity was localized posteriorly.

The patient continued on a progressive downhill course until death four months after the onset. The autopsy revealed the typical changes of CJD.

Case 3 A 73 year old male was admitted to hospital with a one month history of aggressive paranoid behaviour, episodic confusion and formed visual hallucinations. The patient was disoriented and cranial nerve function was normal except for a left visual field neglect. There was a left-sided limb apraxia associated with a diffuse left sensory inattention. A CT scan of the brain revealed diffuse cerebral atrophy. An EEG showed diffuse 7 - 8 Hz low to medium amplitude background rhythm and intermittent periodic 0.8 Hz sharp waves over the right hemisphere, maximum posteriorly (Figure 3A). Lower amplitude discharges were reflected synchronously over homologous regions on the left. His response to verbal commands was appropriate and when he spoke there was attenuation of the sharp wave complexes.

Over the next three weeks, the visual hallucinations persisted, his level of consciousness diminished and bilateral myoclonic movements appeared. In the second EEG done 20 days after the initial record, with the patient in a stuporous state, 5 - 6 Hz diffuse oligorhythmic activity was the dominant rhythm. There were occasional periodic bi-occipital synchronous sharp waves. No cerebral discharges correlated with the rare myoclonic jerking. There was progressive deterioration with the appearance of a left hemiparesis, generalized rigidity, and stimulus sensitive myoclonus. A third EEG, six weeks after the initial record revealed occasional disorganized 5 - 6 Hz activity with prolonged periodic 0.8 - 1 Hz synchronous bihemispheric spikes and sharp waves (Figure 3B). Tactile stimulus sensitive myoclonus obscured the peri-

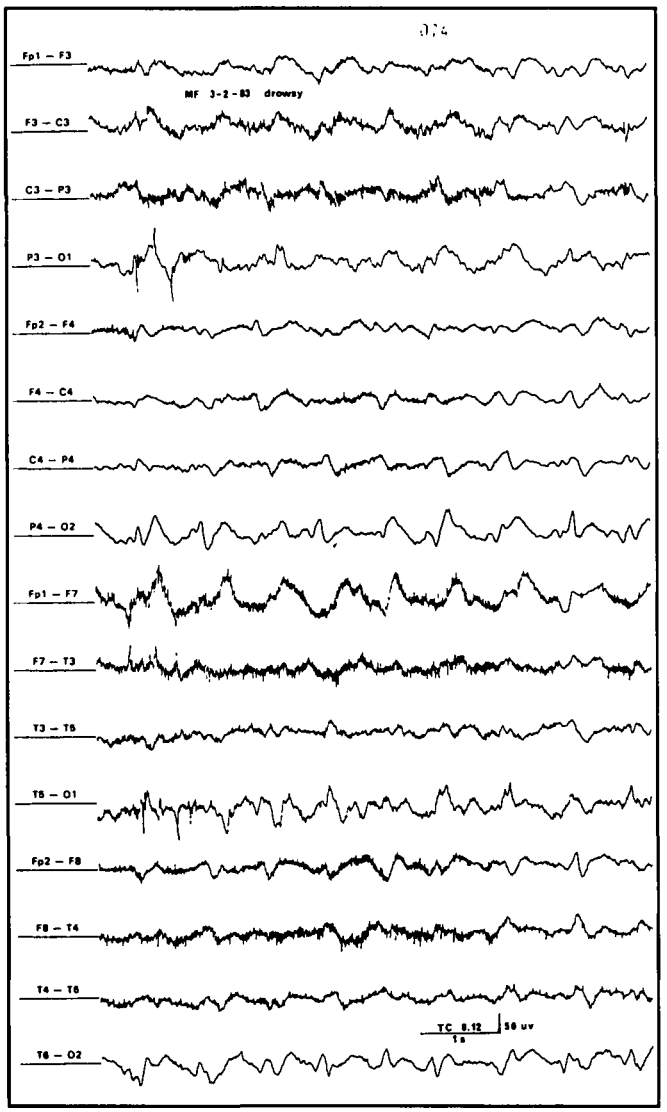

Figure 2 — Case 2
(A) On admission, infrequent periodic 0.5 - 0.8 Hz sharp waves are confined to the right occipital region and there is diffuse background slowing.

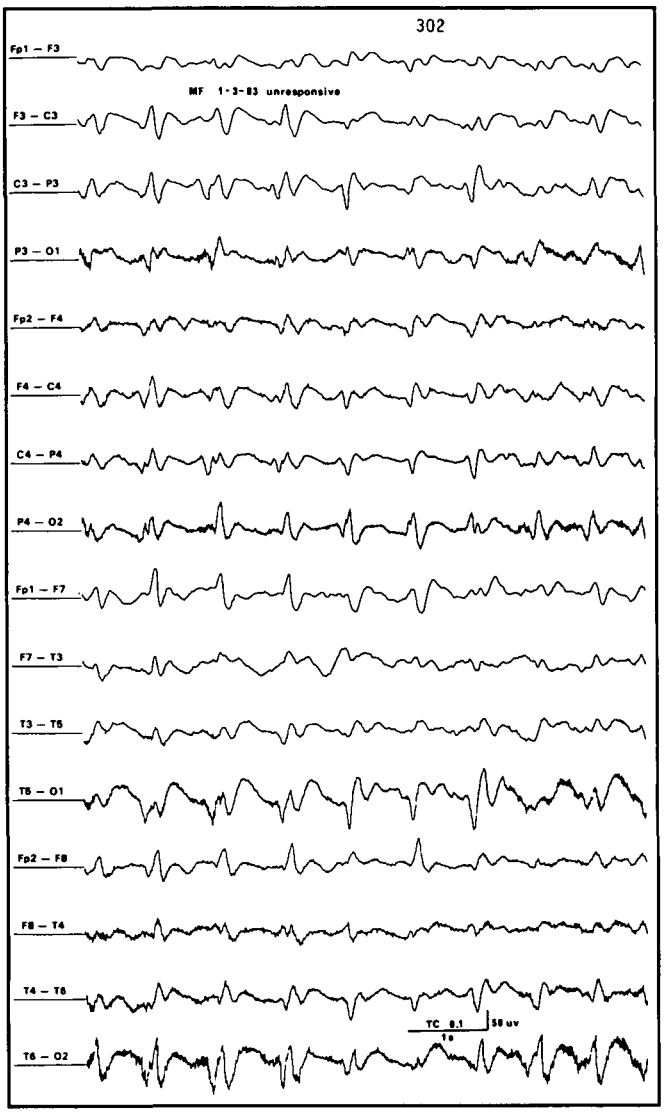

Figure 2— Case 2
(B) One month later the EEG shows continuous periodic 0.8 - 1 Hz epileptiform discharges over both hemispheres.

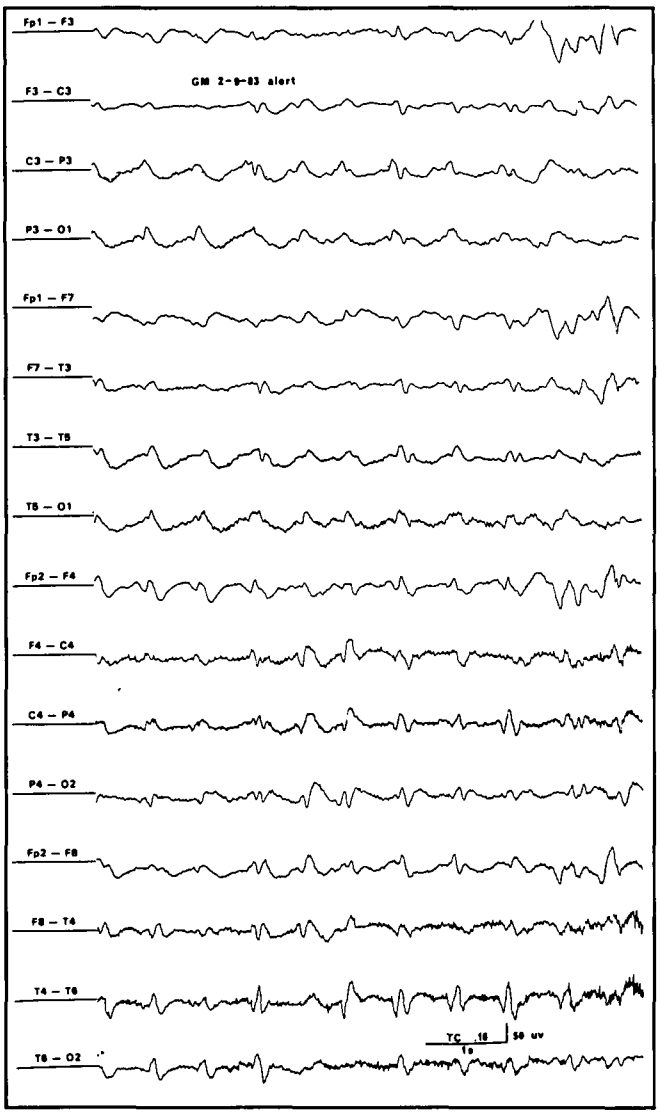

Figure 3— Case 3

(A) Intermittent periodic 0.8 Hz sharp waves are present over the right hemisphere, maximum posteriorly, in the first EEG one month after onset of symptoms. The sharp waves are reflected synchronously over homologous regions on the left where they are of lower amplitude.

odic epileptiform complexes by diffuse muscle artifact or rhythmic 3 -4 Hz activity.

In the final recording 10 days later, there was no significant change other than more frequent myoclonus induced artifact, obscuring the cerebral potentials. The patient remained in a stuporous state and died 4 ½ months after the onset of the illness. The autopsy revealed the typical changes of CJD.

Discussion

Bisynchronous periodic EEG discharges are seen in more than 75% of cases of CJD.[2] Chiappa et al[8] reported periodic complexes in 18 of 19 patients with pathologically verified CJD within 12 weeks of the onset of symptoms. The authors felt that the absence of such a pattern after 12 weeks should suggest another diagnosis.

Similar bisynchronous discharges are occasionally seen with anoxic encephalopathy.[9] Watson[10] reported a case of Alzheimer's disease with clinical and electroencephalographic features similar to those of CJD. However, the periodicity of the synchronous epileptiform complexes was 4 - 9 Hz. In CJD the paroxysmal discharges recur at an exceedingly regular rate with a periodicity of one second or slightly less.[11]

Initial focal slowing is not unusual in CJD[3] and may suggest localized disease. The EEG eventually becomes diffusely slow. Lateralization of the periodic complexes is more unusual but has been described.[5-7] PLEDS are more commonly associated with acute unilateral lesions such as infarcts and tumors, but are also seen with brain abscesses and herpes simplex encephalitis.[12-14] PLEDS may also be seen in chronic seizure disorders or static lesions complicated by recent seizures, alcohol withdrawal or toxic metabolic disorders.[15] In most cases the voltage and frequency of the PLEDS tend to decrease with time and eventually after several weeks, they disappear.[12] In herpes simplex encephalitis, however, they may become bilateral as the disease progresses.[13-14] The emergence of periodic complexes in herpes encephalitis predicts an unfavorable prognosis.[13]

The patients reported here all developed fairly typical clinical patterns of CJD that have been well summarized.[16,17] They presented with focal lateralizing neurologic symptoms and in one the onset was acute and unassociated with dementia. Focal disturbances, especially those involving higher cortical functions, vision, and ataxia may precede the dementia that eventually develops in all patients[17,6,18] and in 10% these symptoms may begin acutely.[16]

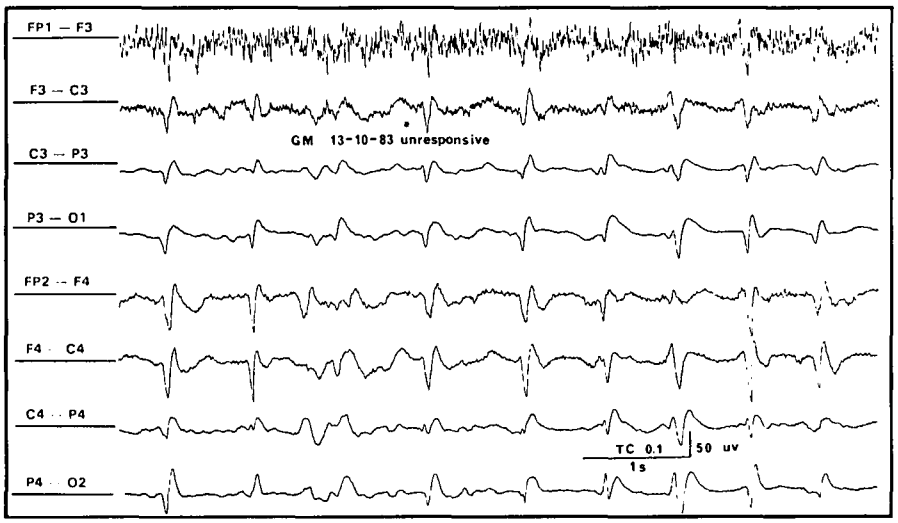

Figure 3 — Case 3

(B) Late in the disease the background is slow, disorganized and low voltage. Continuous spikes and sharp waves with a periodicity of 0.8 - 1 Hz are present bilaterally.

There was good correlation between the initial focal neurologic manifestations and the focal EEG abnormalities. In our three patients, the diagnosis of CJD was not suspected at presentation. In all cases, diffuse background slowing with continuous bisynchronous periodic discharges over both hemispheres coincided with further clinical progression. There was no correlation with the pathologic involvement which was essentially diffuse in all cases. In only one report[6] was the site of the initial PLEDS correlated with the area of maximal pathologic involvement. This was a case of the Heidenhain's variant in which the major pathologic involvement was in the left occipital lobe corresponding to the initial left occipital PLEDS. The pathologic involvement in CJD is usually diffuse in the cerebral cortex and subcortical grey matter. However, there are variants like Heidenhain's[19] and the ataxic form[18] where there are focal differences in severity.

We wish to emphasize that focal EEG abnormalities including PLEDS may precede the more classical electroencephalographic changes in CJD and may suggest other more localized etiologies. However as the disease advances, the presence of periodic sharp waves at a frequency of around 1 Hz in individuals with progressive dementia and myoclonus provides a strong basis for the diagnosis of CJD.

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